CLAIMS

1. Method for evolving a protein X so as to modify its characteristics comprising the following stages:

a) obtaining mutants X* from the sequence coding for the protein X by random mutagenesis;

b) transformation of cells comprising a phenotype [P-] with vectors comprising the mutated nucleic acids obtained in stage a) coding for the proteins X*, P-signifying that said cells are auxotrophic for the substance P, P being the product of the action of X on its natural substrate S;

c) culture of said cells in a medium comprising a substrate S*, S* being an analogue of the natural substrate S of protein X;

d) selection of the cells [P-:: X*] which have survived stage c) in which the proteins X* are capable of carrying out the biosynthesis of the product P from the substrate S.

2. Method according to claim 1, characterized in that the mutant protein X* obtained is a protein having an activity similar to the natural protein X, X* and X belonging to common or neighbouring enzyme classes having at least the first three figures of the 4-figure EC international nomenclature classes.

3. Method according to one of claims 1 and 2, characterized in that the cells used in stage b) are obtained by inactivation of at least one gene involved in the natural metabolic pathway leading to product P.

4. Method according to claim 3, characterized in that the protein X* complements the deficiency of the natural metabolic pathway leading to product P in a medium provided with substrate S*.

5. Method according to one of claims 1 to 4, characterized in that the activity of protein X on substrate S is at least 2 times greater than its activity on substrate S*.

6. Method according to one of claims 1 to 5, characterized in that the activity of protein X* on substrate S* is at least 10 times greater than its activity on substrate S.

7. Method according to one of claims 1 to 6, characterized in that protein X is selected from the ribosyltransferases belonging to the EC classes 2.4.2. -, in particular the N-deoxyribosyltransferases of EC class 2.4.2.6.

8. Method according to one of claims 1 to 6, characterized in that the random mutagenesis of stage a) is carried out either by variation of the manganese concentration during the PCR reaction, or by use of promutagenic nucleotide analogues or also by the use of primers comprising a random sequence.

9. Method according to one of claims 1 to 8, characterized in that said cells are procaryotic or eucaryotic cells, preferably *E. coli*.

10. Method according to one of claims 1 to 9 for evolving an N-deoxyribosyltransferase (DTP) so as to obtain an N-dideoxyribosyltransferase characterized in that it comprises the following stages:

a) obtaining DTP* mutants with the sequence coding for an N-deoxyribosyltransferase (DTP) by random mutagenesis;

b) transformation of cells comprising an [N-] phenotype with vectors comprising the mutated nucleic acids obtained in stage a) coding for the DTP* proteins, N- signifying that said cells are auxotrophic for at least one nucleoside, said nucleoside being the product of the action of DTP on its natural substrate dR-N;

c) culture of said cells in a medium comprising a substrate ddR-N;

d) selection of the [N-:: DTP*] cells which have survived stage c) in which the DTP* proteins are capable of carrying out the transfer of the dideoxyribose (ddR) from a dideoxyribonucleoside to another nucleoside leading to the production of the N nucleoside necessary for the survival of the cells.

11. Method according to claim 10 characterized in that the N-deoxyribosyltransferase (DTP) is the DTP of *Lactobacillus leichmannii* of SEQ ID No 1.

12. Method according to one of claims 10 and 11 characterized in that the cells used in stage b) are *ΔpyrC, Δcod A, Δcdd E.coli* bacteria deficient in the metabolic pathway leading to uracil.

13. Mutated protein X* capable of being obtained by the method according to one of claims 1 to 12, characterized in that it has a modified activity relative to the initial protein X.

14. Mutated N-deoxyribosyltransferase capable of being obtained by the method according to one of claims 1 to 12, characterized in that it has an N-dideoxyribosyltransferase activity and/or an activity on deoxy or dideoxyribonucleoside analogues comprising a modified base.

15. Mutated N-deoxyribosyltransferase according to claim 14 characterized in that it comprises the sequence SEQ ID No 2 comprising the mutation G9S and in that it has an N-dideoxyribosyltransferase activity.

16. Nucleic acid comprising a sequence coding for N-dideoxyribosyltransferase according to claim 15, in particular the sequence SEQ ID No 3.

17. Expression vector comprising a coding sequence according to claim 16.

18. Vector according to claim 17, characterized in that said sequence is fused to an effective promoter in eucaryotic and/or procaryotic cells.

19. Vector according to one of claims 17 and 18, characterized in that it is a plasmid capable of transforming and remaining in *E. coli*.

20. Host cell comprising a vector according to one of claims 17 to 19.

21. Use of an N-dideoxyribosyltransferase according to one of claims 14 and 15 for the transfer of a dideoxyribose (ddR) from a dideoxyribonucleoside to another nucleoside

22. Use according to claim 21 for the preparation of nucleoside or nucleotide analogues having anti-tumorous properties.

23. Use according to claim 21 for the preparation of ddI or ddC.

24. Method for the preparation of compounds comprising a stage consisting of utilizing a mutated protein according to one of claims 13 to 15.

25. Method according to claim 24 for the preparation of nucleoside or nucleotide analogues useful for the treatment of cancer or infectious diseases, in particular dideoxyribonucleosides, in particular ddC and ddI.

26. PAK 9 strain of *E. coli* of genotype *ΔpyrC:: Gm, ΔcodA::Km, cdd::Tn10* deposited at the CNCM under accession number 1-2902.